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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,777	04/09/2004	Glauco P. Tocchini-Valentini	911076.90023	1445

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
10/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

Office Action Summary	Application No.	Applicant(s)	
	10/821,777	TOCCHINI-VALENTINI ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-23* is/are pending in the application.

4a) Of the above claim(s) *18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 19, 2010 has been entered.

Status of Claims

Claims 1 and 4-23 are pending in the instant application. Claims 18-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 8, 2007. Accordingly, claims 1 and 4-17 are currently under examination on the merits in the instant case.

Response to Arguments

Applicant's arguments and the declaration with respect to claims 1 and 4-17 filed with the RCE have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 4-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 4-17 require two independent, separate bulges, one bulge having a guanine/adenine and the other having a uracil/adenine. With regard to the bulge-helix-bulge conformation, the instant specification teaches that one bulge is located in one strand and the other bulge is located in the other, opposite strand. See paragraph 0035. However, claims 1 and 4-11 recite that the BHB conformation is "obtained by hybridizing the target RNA with an oligonucleotide designed to form a bulge-helix-bulge conformation", and claims 12-17 recite that the BHB conformation is "created by two RNA molecules", wherein one of the two RNA molecules is the target RNA (mRNA) molecule. As such, in order to create or obtain a BHB conformation as claimed in the instant case, the target RNA (mRNA) must inherently possess a bulge having either G/A or U/A, independent from the synthetic oligonucleotide (claims 1 and 4-11) or the second RNA molecule (claims 12-17). However, the claims do require that "the target RNA molecule is in a bulge-helix-bulge conformation", thereby requiring that the single strand of target RNA comprises both bulges, which is inconsistent with the description of the BHB conformation provided in the instant specification (e.g., paragraph 0035; Figure 14A). Hence, given the ambiguous claim language, one of ordinary skill in the art cannot ascertain the precise structure of the final BHB conformation obtained or created for the claimed methods, thereby rendering the claims indefinite.

Claims 12-17 require "two RNA molecules" comprising "first" RNA molecule and "second" RNA molecule. Claim 12 recites that the "first" RNA molecule comprises a target

RNA molecule; however, it does not recite what constitutes the "second" RNA molecule. Although claim 13 recites that the two (first and second) RNA molecules are mRNA molecules, it remains unclear what type of mRNA molecule is contained within the "second" RNA molecule. Is it the same "target" RNA? Further, claim 12 requires that the BHB structure is "created" by the first and second RNA molecules. However, if the "first" RNA molecule is a target RNA molecule (thus an mRNA molecule), the "second" RNA molecule cannot be an mRNA molecule as required by claim 13 because the "second" RNA molecule must comprise a nucleotide sequence that is partially complementary to the "first" RNA molecule, thereby creating two bulges on different strands. As such, the essential elements required to perform the claimed methods are vague and unclear, thereby rendering the claims indefinite.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 4-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered when analyzing claims for compliance with the written description requirement include: A) actual reduction to practice; B) disclosure of drawings or structural chemical formulas; C) sufficient relevant identifying characteristics (e.g., complete

structure, partial structure, physical and/or chemical properties, structure/function correlation); D) method of making the claimed invention; E) level of skill and knowledge in the art; and F) predictability in the art.

The claims broadly encompass both *in vitro* and *in vivo* target cleavage methods comprising cleaving both endogenous and exogenous target mRNAs in cells, wherein the cells include mammalian cells located in any mammalian organ including a human organ. Further, claims 1 and 4-11 specifically require an "eukaryotic tRNA splicing endonuclease", whereas claims 12-17 specifically require "heterologous archael tRNA splicing endonuclease".

The instant specification describes that one can artificially introduce or insert a BHB conformation-containing structure into a FLAG-EGFP construct. See Figure 5. This description is not what is claimed in the instant case, which cleaves target RNA (mRNA) by creating or obtaining a BHB conformation with already existing target RNA (mRNA). That is, the splicing of EGFP described in Figures 6-12 does not comprise the claimed method steps and elements. Figure 14 appears to demonstrate a target cleavage method corresponding in scope with the instant claims. Note the ambiguous claim language noted in the 112, second paragraph rejections. However, Figure 14 describes exogenous (not endogenous) target mRNA, firefly luciferase, cleavage in NIH3T3 cells *in vitro* by co-transfecting the firefly luciferase construct and the targeting RNA construct and by exposing the NIH3T3 cells to the archeobacterium *Metahnococcus Jannaschii* endonuclease. See paragraph 00131.

Note that the declarant in the declaration under 37 CFR 1.132 filed on January 19, 2010 has stated that the it was "neither known, nor predictable" or it "was not known or at all predictable", at the time of filing, that a trans-formed BHB could "result in cleavage of an RNA molecule by eukaryal tRNA endonucleases." (emphasis added). See paragraphs 6 and 11.

Hence, given the declaratory statement acknowledging the level of unpredictability and lack of knowledge pertaining to the claimed "trans-formed BHB"-mediated target cleavage, especially by eukaryl tRNA endonuclease claimed in claims 1 and 4-11 at the time of filing, further in view of a single working example showing the exogenous target cleavage in cultured cells *in vitro* with archeobacterium MJ endonuclease, it is concluded that the single species shown in the instant application is not representative of the various species encompassed by the genus claims. Note that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004): "[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated." (emphasis added). See also MPEP §2163.

In light of the above, the instant specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented and were in possession of the genus claimed in the instant case at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low (Acting SPE) can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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